Reversal of dysregulated myelopoiesis in breast cancers and cancer stem cells to boost antitumor immunotherapy

Grant Award Details

Reversal of dysregulated myelopoiesis in breast cancers and cancer stem cells to boost antitumor immunotherapy

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-14166

Investigator:

Name:	Richard Pietras
Institution:	University of California, Los Angeles
Type:	PI

Award Value: $2,327,680

Status: Pre-Active

Grant Application Details

Application Title: Reversal of dysregulated myelopoiesis in breast cancers and cancer stem cells to boost antitumor immunotherapy

Public Abstract:

Research Objective

A new antiestrogen drug will be developed to stop breast cancer (BC) by direct effects on BC cells including stem cells and indirect action on specific procancer immune cells that surround the cancer.

Impact

Substantial numbers of patients with localized breast cancer (BC) and essentially all patients with advanced BC become resistant to current endocrine therapies. New therapeutic strategies are needed.

Major Proposed Activities

- Synthesize sufficient amounts of a purified antiestrogen drug candidate in the chemistry laboratory for use in preclinical work to assess antitumor efficacy and safety in the oncology laboratory.
- Validate antiestrogen properties of a lead SERD candidate, including specific estrogen receptor (ER) binding, elimination of tumor ER and blockade of breast cancer progression in preclinical models.
- Assess effect of estrogens on hematopoietic stem/progenitor cells and expansion of myeloid-derived suppressor cells in bone marrow samples from breast cancer patients and antagonist actions of SERDs.
- Assess antitumor action of SERDs alone and with immunotherapy in diverse breast cancers in preclinical models, with transcriptome sequencing of tumors and assays of the immune tumor microenvironment.
- Characterize myeloid-derived suppressor cell markers and estrogen receptor expression in retrospectively-collected, de-identified breast cancer specimens including ER-positive breast cancer and TNBCs.

Statement of Benefit to California:

This project aims to assess biologic factors that impact racial/ethnic disparities in breast cancer (BC) mortality and address unmet medical needs of diverse California populations, including underserved communities. African American women are almost twice as likely to die from BC vs. European Americans and are often diagnosed with aggressive TNBCs. The proposed work may allow better understanding of racial/ethnic differences in BCs and lead to more effective therapies to benefit Californians.
